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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,618	04/21/2006	Ronny Schulz	KUK-06101	4328
24131 7590 11/12/2009 LERNER GREENBERG STEMER LLP P O BOX 2480 HOLLYWOOD, FL 33022-2480			EXAMINER HOBBS, MICHAEL L	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/576,618

Applicant(s)

SCHULZ ET AL.

Examiner

MICHAEL HOBBS

Art Unit

1797

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 June 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 120-131 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 120-131 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SE/US)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's amendment filed on 06/22/2009 has been considered and entered for the record.

Preliminary Remarks

2. Applicant's amendment overcomes the objection to the specification in paragraph 3 of the Office Action mailed on 01/22/2009. Applicant's amendment overcomes the 35 USC 102(b) and 102(e) rejections in paragraphs 7, 10, 14, 17 and 23 and the 35 USC 103(a) rejection in paragraphs 31, 42, 45, 49 and 54.
3. Newly presented claims 120-131 are pending examination upon the merits.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 120, 121, 125, 129, 130 and 131 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bader (WO 2003/060055) (where US 2005/0084954 A1 is the closest English translation) in views of Rendina (US 3,318,154) and Spaulding (US 6,001,643).

8. Bader discloses a device for cultivating cells that includes for claim 120 a receptacle (receptacle 1) or bioreactor body that comprises the receptacle, a lid (lid 3) and a lower lid (lid 12) or bottom (Fig. 13) and is being interpreted as a basic bioreactor body. Culture medium is delivered to the receptacle by inlet and outlet bores (bores 8 & 9) or hose connectors and force is applied to the cells within the receptacle by means of a magnetized pressure disk or piston (piston 25; [0045]; [0068]). Also, the implant can be supported on a film (film 40; [0082]) that can be peeled off like a plaster and allows the cultivated implant to be easily removed and used. The pressure disk (disk 25) is a magnetizable disk that is connected electrically to the container ([0068]) where this pressure disk applies a pressure to the implant (implant 7) within the bioreactor body.

The means for actuating the pressure disk is an electromagnet (magnet 24) that can be placed outside of the lid (lid 3; [0072]) and is being interpreted as the steering magnet of the instant application. Bader further discloses that the disk has drill holes (holes 26) within the disk and that this allows culture medium to pass through the disk ([0070]).

9. However, claim 120 differs from Bader in that the openings are positioned on the edge of the disk and that the disk includes a vertical guiding edge. Claim 120 further differs from Bader in that the actuator has a magnetic core encapsulated within a biocompatible covering. While this is implied by the reference, Bader does not specify how the disk is magnetizable (electromagnet in the core, a ferro magnetic material in the core).

10. Rendia discloses a sampling apparatus that includes a piston used to introduce on sample fluid with another. For claim 120, Rendia discloses a flow channel in the periphery or edge of the piston (channel 70) that allows fluid to flow from the sample chamber (chamber 24) to an outlet (outlet 78; col. 3 lines 32-40). Further, the piston (piston 16) includes guides or o-rings (rings 48 & 40) for guiding the piston within the sample chamber. With regards to the flow optimization of the culture medium, Bader discloses holes that are fully capable of optimizing the flow of culture medium between the sections of the reactor chamber divided by the actuator. As to the placement of the channel, Rendina demonstrates that the positioning of the channels either interior or to the perimeter of the piston is an engineering design choice that, barring any alleged unexpected results, does not modify the operation of the device in a way that distinguishes over the prior art. Therefore, it would have been obvious to one of

ordinary skill in the art to employ the channel positioning suggested by Rendia within Bader in order to obtain the predictable result of allowing culture medium to move through the pressure disk.

11. Claim 120 differs from the combined teachings of Bader and Rendia in that the pressure disk encapsulates a magnetic core.

12. Spaulding discloses a roller bottle used for culturing three-dimensional cells that for claim 120 includes a control rod (rod 11) or piston that includes a magnet (magnet 10) embedded within the control rod where the control rod is constructed of a polymer suitable for tissue culturing (col. 14 lines 2-4). The rod engages the tissue culture once the electro-magnet is energized providing a force to the cells in order to simulate *in vivo* conditions for the tissue culture. Therefore, it would have been obvious to one of ordinary skill in the art to employ the encapsulated magnet as suggested by Spaulding in order to provide a compressive force to the cells of Bader and Rendia with a reasonable expectation of success.

13. With regards to claim 121, the "steering magnet" of Bader is fully capable of moving in an upward and downward motion in relation to the polarity of the pressure disk.

14. Regarding the plurality of bore holes for feeding and removing culture medium for claim 125, the embodiment shown in Figure 13 only has one bore for the culture feed and removal. However, the embodiment disclosed in Figure 2 includes two inlets (inlet 8) and outlets (outlets 9) for providing and removing a culture medium from the bioreactor body ([0048]) and that this is a conventional set-up for circulating a culture

medium through a bioreactor. Therefore, it would have been obvious for one of ordinary skill in the art to employ the two inlets and outlets disclosed in this embodiment of Bader with the single inlet and outlet as shown in Figure 13 in order to obtain the predictable result of increased flow into and out of the bioreactor. Furthermore, it is noted that duplication of parts (one inlet and outlet versus two inlets and outlets) with no presentation of a new or unexpected result over the prior art has no patentable significance, consult *In re Harza*, 247 F.2d 669, 124 USPQ 378 (CCPA 1960) and MPEP § 2144.04 VI (B).

15. Regarding claim 130, the combined teachings of Bader, Rendina and Spaulding do not specify that the pole of the interior magnet is oriented in a vertical north pole/south pole orientation. However, the orientation of the magnet is a matter of design choice that would be obvious to one of ordinary skill in the art absent any evidence or alleged unexpected results that the this particular orientation is significant and is therefore a rearrangement of parts (see also MPEP 2144.04 VI B).

16. With regards to claims 129 and 131, the mesh on the magnetic disk is being interpreted as being inert and since it allows for culture medium to pass through the disk, the mesh is being interpreted as wide-meshed, light and fluid and gas permeable (Fig. 13b; [0071]).

17. Claims 122-124 and 128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bader (WO 2003/060055) (where US 2005/0084954 A1 is the closest

English translation) in views of Rendina (US 3,318,154) and Spaulding (US 6,001,643) as applied above and in further view of Takagi et al. (US 2004/0235150 A1).

18. Bader, Rendina and Spaulding are silent regarding the limitations of claims 122-124.

19. With regards to claim 122, Takagi discloses magnets (36) with a rectangular cross-sectional area that are used to rotate the interior magnets (magnets 22) of the disk. While not specifying that these magnets are permanent, the magnets of Takagi are being interpreted as permanent magnets. Furthermore, Takagi discloses a motor (motor 40) that is mounted and adjusted with a fixed tool (bolt guide 44) or slide that is used 'to adjust the height of the motor ([0041]). Also, the rectangular shape of the magnet holder is a engineering design choice barring any presentation of any unexpected results and would be within the skills of one of ordinary skill in the art to incorporate within Bader, Rendina, Spaulding and Takagi. With regards to the compression being controlled by a permanent magnet, there are a finite means to control the compression of the pressing plate or piston that includes an electromagnet, a permanent magnet or a pair of electromagnets to regulate the amount of force applied to the cell matrix. Therefore, it would have been obvious to one of ordinary skill in the art to employ the magnets suggested by Takagi in place of the electromagnet of Bader, Rendina and Spaulding with a reasonable expectation of success.

20. With regards to claims 123, and 124 Takagi discloses more than one magnet and are in a disk shaped holder (Fig. 14) that can be adjusted in the vertical direction and the motor (motor 40) is being interpreted as a step motor. Following the reasoning used

for claim 122, it would be obvious to one of ordinary skill in the art to employ circular holder as suggested by Takagi in order to apply a force to the matrix of Bader, Rendina and Spaulding with a reasonable expectation of success.

21. Regarding claim 128, Bader, Rendina and Spaulding are silent regarding the floor of the reactor being transparent.

22. Takagi discloses for claim 128 that the chamber is a single chamber and the cells are "stimulated" on the floor of the bioreactor (Fig. 1) and has a circular or cylindrical shape (Fig. 14). Also, the wall (wall 128) or bottom of the reactor is transparent to allow optical observation by a CCD camera (camera 130; [0075]). The transparent floor and CCD camera of Takagi solves the problem of the instant application by allowing the cells being cultured to be observed and adjustments made to the culture by a control unit ([0075]). Therefore, it would have been obvious to one of ordinary skill in the art to employ the transparent bottom and CCD Camera of Takagi within the reactor of Bader, Rendina and Spaulding in order to observe the growth of the cells. The suggestion for doing so at the time would have been in order to monitor the proliferation and growth of the cells and the appropriate processing of the cells can be executed according to the state the cells are in ([0076]).

23. Claims 126 and 127 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bader (WO 2003/060055) (where US 2005/0084954 A1 is the closest English translation) in view of Rendina (US 3,318,154) and Spaulding (US 6,001,643) as applied above and in further view of Altman et al. (US 2004/0219659 A1).

24. Bader, Rendina and Spaulding are silent regarding a 3-way valve or a sampling taking section.

25. For claim 126, Altman discloses a three way valve that directs the culture media to either the perfusion inlet or the sheath inlet (Fig. 1). Furthermore, the valve of Altman also functions as a three-way valve for the discharge from the bottom of the reactor (see Fig. 1). Therefore, it would be obvious to one of ordinary skill in the art to employ the "three-way" valve as suggested by Altman in order to send the culture medium to the bioreactor of Bader, Rendina and Spaulding. The suggestion for doing so at the time would have been in order to send the perfusate to the one or more inlets of the bioreactor ([0012]).

26. With regards to claim 127, both Bader and Altman are silent regarding a sampling port being part of the discharge section. However, it would be an obvious modification of the valves of Altman for one of ordinary skill in the art to employ a sampling port for the bioreactor of Bader.

Response to Arguments

27. Applicant's arguments with respect to claims 120-131 have been considered but are moot in view of the new ground(s) of rejection.

28. The new grounds of rejection are in view of Rendina which corrects the deficiency within the applied reference of Bader regarding the positioning of the drill holes for allowing culture media to flow through the pressure disk.

Conclusion

29. No claims are allowed.
30. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **MICHAEL HOBBS** whose telephone number is (571)270-3724. The examiner can normally be reached on Monday-Thursday 7:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Marcheschi can be reached on (571) 272-1374. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M. H./
Examiner, Art Unit 1797

/William H. Beisner/
Primary Examiner, Art Unit 1797